## REMARKS

With this reply, Applicants have amended claims 1, 2, and 9-11, and cancelled claims 3-8, 12, and 13. Accordingly, upon entry of this Amendment claims 1, 2, and 9-11 are pending in this application.

Support for the amendment of claims 1 and 2 can be found, for example, on pages 16 and 17 of the specification, Example 7(b), and original claim 3. Claims 9 and 10 have been amended to change their dependencies. Claim 11 has been amended to recite a method of treatment. All claim amendments are made without prejudice. The amendments do not add new matter and their entry is respectfully requested.

Priority

Attached to this Response is an Application Data Sheet, which complies with 37 C.F.R §§ 1.63(c) and 1.76 and acknowledges the filing of European Patent Application No. 02016440.6. Applicants respectfully request entry of this data.

Drawings

The Examiner objected to a panel of Figure 5 due to a typographical error. Applicants will correct this figure at a later date and respectfully request that the objection be held in abeyance until the identification of allowable subject matter.

Specification

Applicants have amended the specification, as requested by the Examiner.

Claim objections

Applicants have amended the claims to remove improper multiple dependencies.

Rejections under 35 U.S.C. § 112, second paragraph and 35 U.S.C. § 101

Claim 11 was rejected under 35 U.S.C. § 112, second paragraph and 35 U.S.C. § 101 for failing to set forth any steps in a method/process. Claim 11 has been amended to recite steps in the method, rendering the rejection moot. Accordingly, these rejections may be withdrawn.

Rejections under 35 U.S.C. § 112, first paragraph: enablement

Claims 7, and 9-11

Claims 7 and 9-11 stand rejection under 35 U.S.C. § 112, first paragraph as allegedly not enabled. Specifically, the Examiner alleged that the specification did not provide evidence that the antibodies recited in the claims were 1) known and readily available to the public; 2) reproducible from the written description. Office Action at 5. The cancellation of claim 7 renders its rejection moot. Claims 9-11 no longer recite these elements, rendering their rejection moot as well. Accordingly, this rejection may be withdrawn.

Claim 11

Claim 11 was rejected as allegedly not enabled. Specifically, although the Examiner acknowledges that the specification is enabling for the use of a MUC1 molecule for producing a pharmaceutical composition for the treatment of tumors, the Examiner alleges that the specification does not enable the use of MUC1 for preventing tumors. Office Action at 8. Applicants respectfully traverse.

Without acquiescing to the Examiner's reasoning and solely to facilitate prosecution, amended claim 11 no longer recites the prevention of tumors. Accordingly, the rejection should be withdrawn and the claim reconsidered.

**Novelty**

Claims 1-3 were rejected under 35 U.S.C. § 102(b) as allegedly anticipated by Snijdewint et al., *Cancer Immunol. Immunother* 48:47-55 (1999) (*Snijdewint*), as evidence by Ryuko et al., *Tumor Biol.* 21:197-210 (2000) (*Ryuko*). Specifically, the Examiner alleges that *Snijdewint* reports isolating MUC1 from the supernatant of a breast cancer cell line by molecular size and affinity chromatography, including the use of a MUC1 mAb, 139H2. Office Action ay 13. *Ryuko* was cited to allegedly show that the 139H2 mAb has the properties recited in Applicants' claims, absent evidence to the contrary. *Id.* Applicants respectfully traverse.

The cancellation of claim 3 renders its rejection moot. As amended, claims 1 and 2 recite that the mixture of MUC1 molecules is a cell, or lysate of a cell, which expresses or secretes tumor associated MUC1. *Snijdewint*, in contrast, reports preparation of purified MUC1 from the *supernatant* of a breast cancer cell line. *See Snijdewint* at 48, right column. The supernatant of a cell culture is not a cell line or a lysate of a cell line. Therefore, *Snijdewint* does not teach this feature of the claimed methods.

In addition, *Snijdewint* does not teach that the MUC1 molecules purified from cell culture supernatant are able to *generate* an immune response in humans, as required by the claims. Instead, *Snijdewint* studied the proliferation of PBMCs from patients with and without ovarian cancer in response to purified MUC1 peptides. *Snijdewint* reports the *existence* of "MUC1-antigen-specific T cells in the blood of [some] ovarian cancer patients...," not the *generation* of an immune response. *See Snijdewint* at 51, right column, first full paragraph. Thus, at best, the authors describe a diagnostic test for

pre-existing MUC1-responsive cells, *not* a method of producing MUC1 molecules that *generate* such a response. Moreover, the effect of the purified MUC1 on proliferation of PBMCs from three healthy patients and twelve ovarian cancer patients was, at best, unclear. *See Snijdewint* at 49 "Effect of MUC1 on PBMC proliferation." None of the PBMC samples from healthy patients exhibited *any* proliferation in response to the MUC1 purified from breast tumor cell supernatant while PBMCs from only *three of twelve* ovarian cancer patients proliferated in response to the purified protein. *Id.* Moreover, when co-incubated with *C. albicans*, MUC1 exhibited an *immunosupressive* effect on PBMCs from almost all of the nine ovarian cancer patients tested. *Id.*: "Effect of MUC1 on proliferation of *C. albicans*-stimulated PBMCs." As a result of these studies, the authors conclude that "[t]he weak proliferative responses we found made it *impossible* to find positive or negative correlations [of humoral responses to MUC1 with cellular responses to MUC1 and its tandem repeats]." *Snijdewint* at 53, left column, second full ¶ (emphasis added). Accordingly, *Snijdewint* does not teach a method of producing or identifying a MUC1 molecule which is able to generate an immune response in humans, as required by the amended claims.

The report of the biophysical properties of the 139H2 mAb in *Ryuko* does not remedy either of these defects. Therefore, *Snijdewint* does not teach all elements of Applicants' claims and does not anticipate them. *See, e.g.*, M.P.E.P. § 2131. Accordingly, Applicants respectfully request withdrawal of the rejection and reconsideration of the claims.

Non-obviousness

Claims 1-3, 7, and 9-11 stand rejected under 35 U.S.C. § 103(a) as allegedly obvious over *Snijdewint*, in view of *Ryuko*, and further in view of U.S. Patent Nos. 4,939,240 (*Chu*) and 7,402,403 (*Robertson*). The Examiner acknowledges that *Snijdewint* does not teach isolating MUC1 with the A76-A/C7 antibody or further formulating the molecule in a pharmaceutically or diagnostically acceptable form. Office Action at 14. The Examiner relies on *Ryuko*; and *Chu* and *Robertson* to suggest 1) the antibody used in *Snijdewint* to isolate MUC1 from culture supernatant could be substituted with, e.g., A76-A/C7, since the antibodies allegedly bind the same epitope of MUC1 and have similar reactivity patterns; and 2) methods of formulation of tumor antigens in pharmaceutically or diagnostically applicable form were known in the art, respectively. *Id.* at 16. Applicants traverse.

The pending claims are directed to methods for the production/identification of a MUC1 molecule, which is:

1) isolated from a MUC1 expressing cell or lysate, and

2) able to generate an immune response in humans.

In contrast, as discussed under the previous heading, *Snijdewint* reports purified MUC1 preparations isolated from the supernatant of a MUC1-expressing cell line. *See Snijdewint* at 49, right column, "Effect of MUC1 on PBMC proliferation." These preparations, in turn, were used as diagnostic tools to confirm the presence of MUC1-antigen-specific T cells in the blood of ovarian cancer patients. *Snijdewint* at 51, right column, 1st ¶ "Discussion." *Snijdewint* does not teach or suggest isolating MUC1 from a cell or lysate or even that the MUC1 molecules purified from a tumor cell supernatant

are able to *generate* an immune response in humans. For example, the MUC1 molecules in *Snijdewint* did not induce proliferation of PBMCs from healthy donors, while PBMCs from only three of twelve ovarian cancer patients proliferated in response to this purified MUC1. Moreover, the purified MUC1 in *Snijdewint* had an *immunosupressive* effect on *C. albicans*-stimulated PBMCs from cancer patients. In contrast, Applicants teach that the lysate of a cell line that expresses a MUC1 molecule (*see* Example 5) generates a MUC1-specific cytotoxic immune response (*see* Example 7).

Although *Snijdewint* posits "that modified MUC1 derivatives can be putative candidates for a cancer vaccine" it offers no teaching or suggestion for how to produce such a vaccine (and therefore produce an immune response). *See Snijdewint* at 53, last ¶. In fact, *Snijdewint's* teaching that MUC1 isolated from culture supernatant has an immunosuppressive effect in *C. Albicans*-stimulated PBMCs would lead the skilled artisan away from Applicants' methods of producing MUC1 molecules that *generate* an immune response in humans. *See* M.P.E.P. § 2145(X)(D). Accordingly, it would be improper to combine the disclosure of *Snijdewint* with the other references cited in the rejection to find Applicants methods obvious. Even if the Examiner disagrees, the remaining references, alone or in combination, do not remedy the defects of *Snijdewint* and collectively do not lead the skilled artisan to the claimed methods, let alone with the necessary *reasonable* expectation of success. See M.P.E.P. § 2143.02.

*Ryuko* was cited to allegedly evidence properties of the mAb used in *Snijdewint*. Office Action at 14-15. However, *Ryuko* merely describes generating and characterizing a monoclonal antibody (VU-2-G7) raised to 3M GalNAc and does not

remedy the defects of *Snijdewint*, described above. *See Ryuko* at 198, left column, first full paragraph. The authors of *Ryuko* simply hypothesize that the antigen of VU-2-G7 may be a useful MUC1 glycopeptide for active immunotherapy, based on its binding properties, with no suggestion of how to isolate a MUC1 molecule able to generate an immune response in humans from a cell or cell lysate.

The Examiner cites to two passages in *Chu* to allegedly demonstrate formulation of isolated tumor antigens. Office Action at 15. Although *Chu* reports that a monoclonal antibody referenced as F36/22 recognizes Ductal Carcinoma Antigen (DCA), MUC1 is not mentioned even once in *Chu*. The passages cited by the examiner merely report that 1) purified DCA can be suspended in a saline carrier with or without albumin and administered as a vaccine (col 14, lines 59-63) and 2) the F36/22 antibody can be used to purify DCA from *malignant effusions* from breast cancer patients (col 30, lines 15-18, in particular). DCA is a completely different antigen from MUC1 and reports on how to purify and formulate DCA from malignant effusions, alone or in combination with *Ryuko* and *Snijdewint* offer no teaching or suggestion of how to produce or identify a MUC1 molecule from a cell or lysate, which can generate an immune response in humans.

The Examiner cites to *Robertson* for allegedly describing a human MUC1 preparation obtained from the body fluids of a breast cancer patient. Office Action at 15. *Robertson*, which is directed to methods of diagnosing cancer by detecting tumor markers, only describes isolating MUC1 from the pooled *sera* of patients with advanced breast cancer, not a cell or lysate. *See Robertson* at col 9, lines 50-63. *Robertson* then describes using this known tumor marker as an antigen in an assay to detect auto-antibodies specific to MUC1, not to generate an immune response in humans. See

Robertson at column 7, lines 24 and 25. Thus, *Robertson*, alone or in combination with *Snijdewint*, *Ryuko*, and *Chu* offers no teaching or suggestion to isolate MUC1 from a cell or lysate as required by the claims, nor does it suggest a method of producing MUC1 which can *generate* an immune response—its teachings are limited to diagnostics for detecting autoantibodies.

None of the references cited by the Examiner, alone or in combination, remedy the failure of *Snijdewint* to teach or suggest 1) isolating MUC1 from a *cell or lysate*; 2) which is able to *generate* an immune response in humans. Therefore, the collective disclosure of *Snijdewint, Ryuko*, *Chu*, and *Robertson* does not teach or suggest all elements of Applicants claims and does not render them obvious, and certainly not with the necessary reasonable expectation of success. Withdrawal of the rejection and reconsideration of the claims are respectfully requested.

Please grant any extensions of time required to enter this response and charge any additional required fees to our deposit account 06-0916.

Respectfully submitted,

FINNEGAN, HENDERSON, FARABOW,
GARRETT & DUNNER, L.L.P.

Dated: April 28, 2009

By: _____
Laurence A. Shumway
Reg. No. 61,169
617.452.1689

**Attachment**
Application Data Sheet

# Attachment 1